IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	Confirmation No. 2579
KENTEN et al.	Atty. Ref.: 4504-4
Serial No. 10/726,069	T.C. / Art Unit: 1636
Filed: December 3, 2003	Examiner: J.S. Ketter

FOR: METHODS FOR IDENTIFIYING THE ACTIVITY OF GENE PRODUCTS

* * *

APPEAL BRIEF UNDER 37 CFR § 41.37

Friday, February 12, 2010

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Appellants submit this Brief to appeal the Examiner's final rejections as set forth in his Office Action mailed January 2, 2009 (the "final Office Action"). The fee required under 37 CFR § 41.20(b)(2) is submitted herewith.

The Notice of Appeal was filed on July 2, 2009. The Notice of Panel Decision reset the initial due date for filing this Brief to September 7, 2009. Appellants petition for a five-month extension in the period for response; the required fee is attached. Thus, the extended due date of February 7, 2010 was a Sunday. Since the federal government was closed on February 8-11, 2010, this Brief is timely filed.

Reversal of the Examiner's rejections of claims 1-4, 6-12, 14-19 and 21-29 by the Board of Patent Appeals and Interferences (the "Board") is respectfully requested.

I. REAL PARTY IN INTEREST

The assignee, Meso Scale Technologies LLC, holds all rights in this application, as well as the invention disclosed and claimed therein, by the assignment recorded on July 20, 2004 in the Patent and Trademark Office (PTO) starting at reel 015579 and frame 0400.

II. RELATED APPEALS AND INTERFERENCES

Appellants, the assignee, and the undersigned do not know of any prior or pending appeal, interference, or judicial proceeding which is related to, directly affects or is directly affected by, or has a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

Claims 1-4, 6-12, 14-19 and 21-29 stand rejected, and are at issue in this appeal. They are listed in the Claims Appendix.

Claims 5, 13 and 20 were canceled without prejudice or disclaimer.

IV. STATUS OF AMENDMENTS

An Amendment was submitted under 37 CFR § 1.116 on April 2, 2009. The Examiner stated in his Advisory Action mailed May 15, 2009 that the amendment would be entered.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The invention of the claims involved in this appeal is directed to a method for determining whether a gene product has an activity of interest.

The present claim 1 results from incorporating limitations of original claims 13 and 20 into the original independent claim. It is supported by page 2, line 8, to page 3, line 20, of the specification. Claim 1 requires a method comprising: (a) co-transfecting a cell with (i) a first vector selected from a library of vectors, at least two members of the aid library comprising genes which encode different test proteins, and (ii) a second vector comprising a gene which encodes a reporter protein, wherein the reporter protein affects or regulates a biological process in the cell; (b) expressing the different test proteins and the reporter protein in a transfected cell; (c) measuring abundance and/or activity of the reporter protein by observation of an indicator of the biological process in the transfected cell, wherein the abundance and/or activity of the reporter protein is modulated by the presence of a protein that modulates the reporter protein; and (d) screening the library for one or more members which encode test proteins that modulate the reporter protein.

Dependent claim 2 is directed to a particular embodiment of claim 1 that specifies the first vector and/or the second vector further comprise promoter sequences. It is supported by page 2, line 16, of the specification.

Dependent claim 4 is directed to a particular embodiment of claim 1 that specifies the transfection reagent is at least one of a list of proprietary lipid compositions, which is found at page 12, lines 19-23, of the specification.

Dependent claim 6 is directed to a particular embodiment of claim 1 that specifies that co-transfecting comprises: (i) coating a well of a multi-well plate with a polycation polymer; (ii) contacting the cell with the first vector, the second vector, and the transfection reagent in the well; and (iii) incorporating the first and the second vectors in the cell to produce the transfected cell. It is supported by page 4, line 22, to page 5, line 2; and page 13, lines 1-5, of the specification.

Dependent claim 7 is directed to a particular embodiment of claim 1 that specifies abundance of the reporter protein is measured. It is supported by page 3, line 4, of the specification.

Dependent claim 8 is directed to a particular embodiment of claim 7 that specifies the reporter protein is measured by luminescence. It is supported by page 3, line 10, of the specification.

Dependent claim 9 is directed to a particular embodiment of claim 7 that specifies the reporter protein is measured by a binding assay. It is supported by page 3, line 11, of the specification.

Dependent claim 10 is directed to a particular embodiment of claim 7 that specifies the reporter protein is measured by electrophoretic analysis. It is supported by page 3, line 11, of the specification.

Dependent claim 11 is directed to a particular embodiment of claim 1 that specifies the activity of the reporter protein is an enzymatic activity that catalyzes the reaction of a substrate to form a product, and the enzymatic activity is measured by adding the substrate and measuring consumption of the substrate and/or formation of the product. It is supported by page 3, lines 5-7, of the specification.

Dependent claim 12 is directed to a particular embodiment of claim 11 that specifies the enzyme activity is β-galactosidase activity, β-lactamase activity, or luciferase activity. It is supported by page 3, line 8, of the specification.

Dependent claim 14 is directed to a particular embodiment of claim 1 that specifies the indicator is cell morphology, change in abundance of a native protein, change in post-translational modification of a native protein, change in transcription of a native gene, or change in secretion of a native protein. It is supported by page 3, lines 15-19, of the specification.

Dependent claim 15 is directed to a particular embodiment of claim 1 that specifies the activity of the reporter protein is aggregation and the reporter protein is Sup35. It is supported by page 26, lines 3-4, of the specification.

Dependent claim 16 is directed to a particular embodiment of claim 1 that specifies the activity of interest is pro-apoptotic or anti-apoptotic activity. It is supported by page 5, lines 3-6, of the specification.

Dependent claim 17 is directed to a particular embodiment of claim 1 that specifies the method further comprises: confirming that expression of the test protein results in a change in an indicator of apoptosis by another assay. It is supported by page 5, lines 8-9, of the specification.

Dependent claim 18 is directed to a particular embodiment of claim 17 that specifies the indicator of apoptosis by another assay is DNA fragmentation, caspase activation, annexin staining on the outer membrane, DNA ladder formation, or production of cleavage products of caspase such as DFF45, alpha fodrin, or lamin A. It is supported by page 5, lines 9-11, of the specification.

Dependent claim 19 is directed to a particular embodiment of claim 1 that specifies the method further comprises: repeating the method with another cell having a different genetic background. It is supported by page 5, line 12, of the specification.

Dependent claim 21 is directed to a particular embodiment of claim 1 that specifies the library comprises at least 1000 different genes. It is supported by page 2, line 21, of the specification.

Dependent claim 22 is directed to a particular embodiment of claim 1 that specifies the cell is co-transfected in a multi-well plate. It is supported by page 2, lines 22-23, of the specification.

Dependent claim 23 is directed to a particular embodiment of claim 1 that specifies the method further comprises: (d) repeating the method using a third vector instead of the first vector, the third vector differing from the first vector in that it i) does not code for a protein; ii) codes for a protein that is known to not have the activity of interest or iii) does not have a promoter sequence; and (e) comparing the activity and/or abundance of the reporter protein measured with the first vector and the third vector to determine whether the test protein has the activity of interest. It is supported by page 4, lines 1-7, of the specification.

Dependent claim 24 is directed to a particular embodiment of claim 1 that specifies the method further comprises: (d) repeating the method without the first vector; and (e) comparing the activity and/or abundance of the reporter protein measured with and without the first vector to determine whether the test protein has the activity of interest. It is supported by page 3, line 23, to page 4, line 1; and page 4, lines 5-7, of the specification.

Independent claim 25 is directed to a specific embodiment of the invention using a multi-well plate. It is supported by page 2, line 8, to page 3, line 20; page 4, line 20, to page 5, line 2; and page 8, line 10, to page 9, line 8, of the specification. Claim 25 requires a method comprising: (a) treating a well of a multi-well plate with a transfection reagent; (b) adding to the well (i) a first cell preparation, (ii) a first vector selected from a library of vectors, at least two members of the library comprising genes which encode different test proteins, and (iii) a second vector comprising a gene which encodes a reporter protein, wherein the reporter protein affects or regulates a biological process in the cell; (c) incubating the multi-well plate to allow cells to incorporate the first and the second vectors; (d) expressing the different test proteins and the reporter protein in a transfected cell; (e) measuring abundance and/or activity of the reporter protein by observation of an indicator of the biological process in the transfected cell, wherein the abundance and/or activity of the reporter protein is modulated by the presence of a protein that modulates the reporter protein; (f) screening the library for one or more members which encode test proteins that modulate the reporter protein; and (g) repeating (a) to (e) in an additional well of the multi-well plate with a further cell preparation having the same or different genetic background as the first cell preparation.

Therefore, the invention as presently claimed is clearly supported by Appellants' disclosure as originally filed.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Under 35 U.S.C. 102(b), was it proper to reject claims 1-3, 7 and 21-22 as allegedly anticipated by Gallatin et al. (US 5,728,533)?

B. Under 35 U.S.C. 103(a), was it proper to reject claims 1, 3-4, 6, 8-12, 14-19 and 23-29 as allegedly obvious over Gallatin et al. (US 5,728,533) in view of Hillman et al. (US 5,942,399)?

C. Under 35 U.S.C. 112, 2nd paragraph, was it proper to reject claims 4-5, 14 and 21-22 as allegedly indefinite?

VII. ARGUMENTS

Claims 1-4, 6-12, 14-19 and 21-29 do not stand or fall together because the obviousness rejection was not applied against all of the pending claims and it depends on the additional citation of the '399 patent. Each claim requires the separate comparison of different combinations of limitations against the prior art.

First, assuming the Section 102 rejection is reversed, at least claims 2 and 7 would have no rejection pending against them. Even if the Board sustains the Section 103 rejection, these claims would only be objected to as depending from a rejected claim. Further, claims 21-22 would only be objected to if the Section 112 rejection is also reversed.

Second, if the additional citation of the '399 patent does not justify the Section 103 rejection, then the obviousness rejection should be reversed and at least claims 6, 8-12, 15-19 and 23-24 would only be objected to as depending from a rejected claim and claims 25-29 would be allowed. Further, claims 4 and 14 would only be objected to if the Section 112 rejection is also reversed.

The issues presented above and separately argued below demonstrate that there are independent bases for patentability and the pending claims should be consi-

dered in three groups: (I) claims 1 and 3; (II) claims 2, 7 and 21-22; and (III) claims 4, 6, 8-12, 14-19 and 23-29.

If the Board agrees with Appellants that the three rejections under appeal should be reversed, then all groups of claims should be allowable. But if only Section 102 and Section 112 rejections are reversed, then claims 2, 7 and 21-22 of Group II should be allowable. Finally, if only Section 103 and Section 112 rejection are reversed, then claims 4, 6, 8-12, 14-19 and 23-29 of Group III should be allowable.

35 U.S.C. 102 – Novelty

A claim is anticipated only if each and every limitation as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is claimed. See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Claims 1-3, 7 and 21-22 were rejected under Section 102(b) as allegedly anticipated by Gallatin et al. (US 5,728,533). Appellants traverse.

It was alleged in the Office Action that Gallatin discloses cellular expression of a first construct comprising a reporter gene driven by a promoter and a second DNA sequence from a library, wherein expression of the reporter gene is detected. But Apellants' independent claim 1 requires a method comprising (emphasis added):

(a) co-transfecting a cell with (i) a first vector selected from a library of vectors, at least two members of said library comprising genes which encode different test proteins, and (ii) a second vector comprising a gene which encodes a reporter

protein, wherein said reporter protein affects or regulates a biological process in said cell;

(b) expressing said different test proteins and said reporter protein in a transfected cell;

(c) measuring abundance and/or activity of said reporter protein by observation of an indicator of said biological process in said transfected cell, wherein said abundance and/or activity of said reporter protein is modulated by the presence of a protein that modulates said reporter protein; and

(d) screening said library for one or more members which encode test proteins that modulate said reporter protein.

In order to anticipate claim 1, a reference must teach each and every limitation of the claimed invention. Gallatin does not anticipate this independent claim because the cited patent does not teach screening a *library* of vectors for one or more members that have a desired activity, nor does the cited patent teach the use of a *reporter* protein that affects or regulates a biological process in a cell. In the final Office Action, the Examiner referred to his previous Office Action where both of these limitations were alleged to be taught by Gallatin. This apparently refers to a section of the Office Action mailed April 18, 2008 that cited column 5, second full paragraph (emphasis added):

> A modified version of the foregoing assay may be used in isolating a polynucleotide encoding a protein that binds to α_d by transforming or transfecting appropriate host cells with a DNA construct comprising a reporter gene under the control of a promoter regulated by a transcription factor having a DNA-binding domain and an activating domain, expressing in the host cells a first hybrid DNA sequence encoding a first fusion of part or all of α_d and either the DNA binding domain or the activating domain of the transcription factor, expressing in the host cells a library of second hybrid DNA sequences encoding second fusions of part or all of putative α_d binding

> proteins and the DNA binding domain or activating domain of the transcription factor which is not incorporated in the first fusion, detecting binding of an α_d binding protein to α_d in a particular host cell by detecting the production of reporter gene product in the host cell, and isolating second hybrid DNA sequences encoding α_d binding protein from the particular host cell.

Comparison of the limitations of Appellants' claim 1 and Gallatin's disclosure is facilitated by underlining in the above quotations. Differences between Appellants' claimed method and what was disclosed by Gallatin are clearly evident, particularly with respect to their transfection and expression steps. First, the cited patent describes transfecting host cells with a single DNA construct whereas the transfection in independent claim 1 requires co-transfecting a cell with (a) a first vector selected from a library of vectors and (b) a second vector comprising a gene coding for a reporter protein.

Not only does Gallatin's transfection method differ from Appellants' transfection as required by the present claim 1, but their expression methods also differ. Appellants' claim 1 requires expression of different test proteins and the reporter protein in a transfected cell whereas Gallatin's two expression steps call for expressing a first hybrid DNA sequence encoding a first fusion protein, followed by expressing a library of second hybrid molecules encoding a second fusion. Therefore, the cited patent does not anticipate the present claims.

In his Advisory Action, the Examiner appeared to admit that he gave little weight to Appellants' requirement for a gene that encodes a reporter protein ("With respect to the reporter gene, if it had no effect within the cell, it could not be used to screen or select for the presence of the vector" at page 2). The present claim 1 requires, however, screening the library by identifying which test proteins modulate the reporter protein. The reporter gene must have an effect on the cell. Thus, the Examiner's speculation is

irrelevant to proper construction of Appellants' claims because it is the requirement for modulation by a test protein of the reporter protein that enables the claimed method. Anticipation fails if any claim limitation is not disclosed in the prior art.

Further, those claims depending from an independent claim are also not anticipated by the cited patent because all limitations of independent claim 1 are incorporated in claims depending therefrom. See *In re McCarn*, 101 USPQ 411, 413 (C.C.P.A. 1954). Therefore, Gallatin does not anticipate Appellants' claims.

Claims 2, 7 and 21-22

Since the additional limitations of claims 2, 7 and 21-22 are not anticipated by Gallatin, even if only this rejection and the Section 112 rejection below are reversed, then claims 2, 7 and 21-22 should be allowable because the Examiner did not allege they were obvious under Section 103.

Appellants urge the Board to reverse the Section 102 rejection because all limitations of their claimed invention are not disclosed in the cited patent.

35 U.S.C. 103 – Nonobviousness

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See id. ("Often, it will be necessary for a court

to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See id. at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning"). Thus, a prima facie case of obviousness requires "some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct." *Kahn* at 1335; see *KSR* at 1396. A claim that is directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." Id. Finally, a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 1, 3-4, 6, 8-12, 14-19 and 23-29 were rejected under Section 103(a) as allegedly unpatentable over Gallatin et al. (US 5,728,533) in view of Hillman et al. (US 5,942,399). Appellants traverse.

Claim 1

Gallatin was discussed above. It was alleged in the Office Action that Hillman discloses the additional elements recited in the dependent claims. But Hillman does not address the deficiencies described above with respect to Gallatin's disclosure. Thus, the combination of cited patents does not make obvious Appellants' independent claim 1.

In particular, one of ordinary skill in the art would not have found it obvious from the cited patents (neither individually nor in combination) to co-transfect a cell with a first vector selected from a library of vectors, at least two members of said library comprising

genes which encode different test proteins, and a second vector comprising a gene which encodes a reporter protein, wherein that reporter protein affects or regulates a biological process in said cell. Moreover, there is no evidence to establish the obviousness of modifying the two cited patents, either individually or in combination, to make the present claim 1 with a reasonable expectation of success. Therefore, the failure of Gallatin to disclose Appellants' claimed invention is not remedied by the Examiner's attempt to modify its disclosure with Hillman.

Appellants submit that these features of their claimed invention (e.g., different transcription and expression steps) are sufficient to distinguish claim 1 as patentable over Gallatin and Hillman. It is also submitted that there would be no reasonable expectation of success because the cited patents do not provide evidence that transfection of a cell with two vectors (i.e., co-transfection) is accomplished with a surprisingly high probability although efficiency of the transfection method may be low (see page 9, lines 14-20, specification).

Further, claims depending from claim 1 are also not made obvious by the cited patents because the limitations of an independent claim are incorporated in its dependent claims. Therefore, dependent claims 4, 6, 8-12, 14-19 and 23-24 are patentable over Gallatin in view of Hillman because the combination of cited patents does not make obvious all limitations of independent claim 1. See M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988).

Claim 25

Gallatin was discussed above. It was alleged in the Office Action that Hillman discloses the additional elements recited in the dependent claims. But Hillman does not

address the deficiencies described above with respect to Gallatin's disclosure. Thus, the combination of cited patents does not make obvious Appellants' independent claim 25.

In particular, one of ordinary skill in the art would not have found it obvious from the cited patents (neither individually nor in combination) to co-transfect a cell with a first vector selected from a library of vectors, at least two members of said library comprising genes which encode different test proteins, and a second vector comprising a gene which encodes a reporter protein, wherein that reporter protein affects or regulates a biological process in said cell, in the context of repetitively screening of individual wells of a multi-well plate. Moreover, there is no evidence to establish the obviousness of modifying the two cited patents, either individually or in combination, to make the present claim 25 with a reasonable expectation of success. Therefore, the failure of Gallatin to disclose Appellants' claimed invention is not remedied by the Examiner's attempt to modify its disclosure with Hillman.

Appellants submit that these features of their claimed invention (e.g., different transcription and expression steps) are sufficient to distinguish claim 25 as patentable over Gallatin and Hillman. It is also submitted that there would be no reasonable expectation of success because the cited patents do not provide evidence that transfection of a cell with two vectors (i.e., co-transfection) is accomplished with a surprisingly high probability although efficiency of the transfection method may be low (see page 9, lines 14-20, specification).

Further, claims depending from claim 25 are also not made obvious by the cited patents because the limitations of an independent claim are incorporated in its dependent claims. Therefore, dependent claims 26-29 are patentable over Gallatin in view of

Hillman because the combination of cited patents does not make obvious all limitations of independent claim 25. See M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988).

Claims 4, 6, 8-12, 14-19 and 23-29

Since the additional limitations of claims 4, 6, 8-12, 14-19 and 23-29 are patentable over Gallatin in view of Hillman, even if only this rejection and the Section 112 rejection below are reversed, then claims 4, 6, 8-12, 14-19 and 23-29 should be allowable because the Examiner did not allege they were anticipated under Section 102.

Appellants urge the Board to reverse the Section 103 rejection because their claimed invention would not have been obvious to one of ordinary skill in the art.

35 U.S.C. 112 – Definiteness

Claims 4-5, 14 and 21-22 were rejected under Section 112, second paragraph, as allegedly indefinite. Appellants traverse.

The Examiner objected to the alleged use of trademarks in claim 4, but none are recited therein. As regards the same objection to claim 5, without admitting the present rejection is proper, this claim was canceled without prejudice or disclaimer on October 20, 2008. Therefore, this part of the rejection is moot.

Moreover, claims 14 and 21-22 were objected to as allegedly depending from canceled claims. But they depend from claim 1, which is still pending. Therefore, the remaining part of this rejection is also moot.

Appellants urge the Board to reverse this rejection because the pending claims are clear and definite. They were mooted by previously entered amendments.

Conclusion

For the reasons discussed above, the Examiner's rejections are improper and they should be reversed by the Board. Appellants submit that the pending claims are in condition for allowance and earnestly solicit an early Notice to that effect.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: /Gary R. Tanigawa/
Gary R. Tanigawa
Reg. No. 43,180

901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

VIII. CLAIMS APPENDIX

1. (previously presented) A method for determining whether a gene product has an activity of interest comprising:

(a) co-transfecting a cell with

(i) a first vector selected from a library of vectors, at least two members of said library comprising genes which encode different test proteins, and

(ii) a second vector comprising a gene which encodes a reporter protein, wherein said reporter protein affects or regulates a biological process in said cell;

(b) expressing said different test proteins and said reporter protein in a transfected cell;

(c) measuring abundance and/or activity of said reporter protein by observation of an indicator of said biological process in said transfected cell, wherein said abundance and/or activity of said reporter protein is modulated by the presence of a protein that modulates said reporter protein; and

(d) screening said library for one or more members which encode test proteins that modulate said reporter protein.

2. (original) The method of claim 1, wherein said first vector and/or said second vector further comprise promoter sequences.

3. (original) The method of claim 1, wherein co-transfecting comprises contacting said cell with said first vector, said second vector, and a transfection reagent.

4. (previously presented) The method of claim 3, wherein said transfection reagent is at least one proprietary lipid composition selected from the group consisting of:

(i) a liposome formulation of N,N',N'',N'''-tetramethyl- N,N',N'',N'''-tetrapalmitoylspermine (TM-TPS) and dioleoyl phosphatidylethanolamine (DOPE) in 1:1.5 (M/M) respectively,

(ii) a liposome formulation of N-[1-(2,3-dioleyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTMA) and dioleoyl phophotidylethanolamine (DOPE) in 1:1 (w/w) ratio respectively,

(iii) a liposome formulation of 2,3-dioleyloxy-N-[2(sperminecarboxamido)ethyl]-N,N-dimethyl-1-propanaminium trifluoroacetate (DOSPA) and dioleoyl phosphatidylethanolamine (DOPE) in 3:1 (w/w) ratio respectively,

(iv) a mixture of (+)-N,N [bis (2-hydroxyethyl)]-N-methyl-N-[2,3-di(tetradecanoyloxy)propyl] ammonium iodide and L-dioleoyl phosphatidylethanolamine (DOPE),

(v) a mixture of [N,N,N',N'-tetramethyl-N,N'-bis(2-hydroxyethyl)-2,3-di(oleoyloxy)-1,4-butanediammonium iodide] and L-dioleoyl phosphatidylethanolamine (DOPE), and

(vi) dioctadecylamidoglycyl spermine (DOGS).

Claim 5 (canceled)

6. (previously presented) The method of claim 3, wherein co-transfecting comprises:

(i) coating a well of a multi-well plate with a polycation polymer;

(ii) contacting said cell with said first vector, said second vector, and said transfection reagent in said well; and

(iii) incorporating said first and said second vectors in said cell to produce said transfected cell.

7. (previously presented) The method of claim 1, wherein abundance of said reporter protein is measured.

8. (original) The method of claim 7, wherein said reporter protein is measured by luminescence.

9. (original) The method of claim 7, wherein said reporter protein is measured by a binding assay for said reporter protein.

10. (original) The method of claim 7, wherein said reporter protein is measured by electrophoretic analysis.

11. (previously presented) The method of claim 1, wherein said activity of said reporter protein is an enzymatic activity that catalyzes the reaction of a substrate to form a

product, and said enzymatic activity is measured by adding said substrate and measuring consumption of said substrate and/or formation of said product.

12. (original) The method of claim 11, wherein said enzyme activity is selected from the group consisting of β-galactosidase activity, β-lactamase activity, and luciferase activity.

Claim 13 (canceled)

14. (previously presented) The method of claim 1, wherein said indicator is selected from the group consisting of change is cell morphology, change in abundance of a native protein, change in post-translational modification of a native protein, change in transcription of a native gene, and change in secretion of a native protein.

15. (previously presented) The method of claim 1, wherein said activity of said reporter protein is aggregation and said reporter protein is Sup35.

16. (previously presented) The method of claim 1, wherein said activity of interest is pro-apoptotic or anti-apoptotic activity.

17. (previously presented) The method of claim 1 further comprising: confirming that expression of said test protein results in a change in an indicator of apoptosis by another assay.

18. (original) The method of claim 17, wherein said indicator of apoptosis is selected from the group consisting of DNA fragmentation, caspase activation, annexin staining on the outer membrane, DNA ladder formation, and production of cleavage products of caspase such as DFF45, alpha fodrin, or lamin A.

19. (previously presented) The method of claim 1 further comprising: repeating said method with another cell having a different genetic background.

Claim 20 (canceled)

21. (previously presented) The method of claim 1, wherein said library comprises at least 1000 different genes.

22. (previously presented) The method of claim 1, wherein said cell is co-transfected in a multi-well plate.

23. (previously presented) The method of claim 1 further comprising:

(d) repeating said method using a third vector instead of said first vector, said third vector differing from said first vector in that it

i) does not code for a protein;

ii) codes for a protein that is known to not have the activity of interest or

iii) does not have a promoter sequence; and

(e) comparing the activity and/or abundance of the reporter protein measured with said first vector and said third vector to determine whether said test protein has said activity of interest.

24. (previously presented) The method of claim 1 further comprising:

(d) repeating said method without said first vector; and

(e) comparing the activity and/or abundance of the reporter protein measured with and without said first vector to determine whether said test protein has said activity of interest.

25. (previously presented) A method for determining whether a gene product has an activity of interest comprising:

(a) treating a well of a multi-well plate with a transfection reagent;

(b) adding to said well (i) a first cell preparation, (ii) a first vector selected from a library of vectors, at least two members of said library comprising genes which encode different test proteins, and (iii) a second vector comprising a gene which encodes a reporter protein, wherein said reporter protein affects or regulates a biological process in said cell;

(c) incubating the multi-well plate to allow cells to incorporate the first and the second vectors;

(d) expressing said different test proteins and said reporter protein in a transfected cell;

(e) measuring abundance and/or activity of said reporter protein by observation of an indicator of said biological process in said transfected cell, wherein said abundance and/or activity of said reporter protein is modulated by the presence of a protein that modulates said reporter protein;

(f) screening said library for one or more members which encode test proteins that modulate said reporter protein; and

(g) repeating (a) to (e) in an additional well of said multi-well plate with a further cell preparation having the same or different genetic background as said first cell preparation.

26. (previously presented) The method of claim 25, wherein said library comprises at least 1000 different genes.

27. (previously presented) The method of claim 25, wherein said transfection reagent comprises a lipid preparation.

28. (previously presented) The method of claim 27, wherein said transfection reagent further comprises a targeting moiety.

29. (previously presented) The method of claim 27, wherein said lipid preparation comprises a cationic lipid preparation.

IX. EVIDENCE APPENDIX

None.

X. RELATED PROCEEDINGS APPENDIX

None.